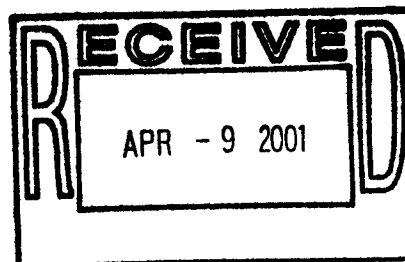


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March 26, 2001

Dr. C.W. Jameson
National Toxicology Program
Report on Carcinogens
MD EC-14 P.O. Box 12233
Research Triangle Park, NC 27709



Dear Dr. Jameson.

I write in support of the listing of steroidal estrogens in the National Toxicology Program's Report on Carcinogens, Tenth Edition.

Steroidal estrogens are known carcinogens. The International Agency for Research on Cancer (IARC) has reported for some time that a large body of evidence in both animal models and humans demonstrates that estrogens cause cancer.

All of us are exposed to estrogens in numerous forms, from animal feed additives to the xenoestrogens in herbicides, pesticides, and plastics. However, women bear a larger burden of exogenous estrogen exposure throughout the life course. From adolescence when estrogens are prescribed for menstrual irregularities and contraception, to childbearing and the use of estrogens to suppress lactation, and to the use of hormone replacement therapy for menopause and osteoporosis, women in industrialized countries have for many years been exposed to significantly higher levels of exogenous estrogens than men.

In particular, according to the National Center for Health Statistics more than 10.4 million U.S. women used oral contraceptives in 1995. A recent article in the Washington Post reported that 8.6 million menopausal women use combination hormone replacement therapy while an additional 12 million women use unopposed estrogen replacement therapy (Washington Post, March 26, 2001). Many women's health activists and others have argued against the widespread use of both these estrogen products, in part because good alternatives are readily available. Samuel Epstein, M.D. has said, "Worldwide use of birth control pills, in spite of conclusive evidence or carcinogenicity of estrogens in experimental animals, constitutes the largest uncontrolled experiment in human carcinogenesis ever undertaken" (Epstein, 1998, 141).

Of particular concern to all women is the possible link between estrogens and breast cancer. More than 182,000 U.S. women are diagnosed each year with invasive breast cancer and more than 40,000 die annually from the disease (American Cancer Society, 2000). In 1940 an

American woman's lifetime risk of breast cancer was 1 in 20. By 1960, the lifetime risk had risen to 1 in 14. By 1988, the risk was 1 in 10 and within a few short years the risk became 1 woman in 8 (Rinzler, 1993).

The risk of breast cancer due to estrogen use increases with length of use, dose amount, and repeated exposures to estrogen. A meta-analysis of more than 50,000 women with breast cancer, reported in *The Lancet* in 1997, demonstrated that the use of hormone replacement therapy (HRT) for 4 years resulted in an excess of one woman with breast cancer for every 1000 woman users. Use of HRT for 13 years resulted in an excess of one woman with breast cancer for every 100 users (Sherman, 2000).

Breast cancer has become a modern day scourge for women, with no clear understanding of its causes or ways to prevent it. In addition to justified concerns regarding steroidal estrogens is the proliferation of xenoestrogens in the larger environment in which we all live. In other words, the context of women's estrogen exposure has, in recent decades, grown far larger than women's own hormone production or the estrogen-containing medications prescribed to women during their lifetimes. As Sandra Steingraber, Ph.D. has pointed out, "Xenoestrogens not only mimic natural estrogens directly but also can indirectly enhance their effects" (in Kasper and Ferguson, 2000, 288). A recent newsletter of the Cornell University Program on Breast Cancer and Environmental Risk Factors in New York State reports on the "alarming increase" of premature thelarche, or premature sexual development among children in Puerto Rico. The authors pose the question of whether estrogenic environmental contaminants are the cause of this phenomenon.

There is at present no way to determine the effects of the full range of accumulated estrogen exposures in the bodies of individual women. The widespread presence of estrogens, their carcinogenic properties, and the epidemic of breast cancer are much-needed and important areas for further research. Furthermore, the most recent issue of the *Journal of the American Medical Association* reports on a 14-year study supported by the American Cancer Society of more than 211,000 women that demonstrated a 2.2 fold increase in the rate of ovarian cancer for women who had taken estrogens for more than 10 years (*JAMA*, March 21, 2001). While we have known about the association of HRT with endometrial cancer and breast cancer, evidence of the link between HRT and ovarian cancer has not been reported until now.

In the interest of protecting the health of all women, the Second World Conference on Breast Cancer adopted the Precautionary Principle, calling for no substance to be released into the environment until its safety has been established (Second World Conference on Breast Cancer, 1999). Listing steroidal estrogens is a wise step towards safeguarding women's health and perhaps reducing the incidence of breast and other cancers.

Yours truly,

A handwritten signature in cursive script that reads "Anne S. Kasper Ph.D.".

Anne S. Kasper, Ph.D.
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